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Dropout is a problem in lifestyle intervention programs for overweight and obese infertile women: a systematic review

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STUDY QUESTION: What are the dropout rates in lifestyle intervention programs (LIPs) for overweight and obese infertile women and can intervention- or patient-related baseline factors associated with dropout be identified in these women?

SUMMARY ANSWER: The median dropout rate was 24% in overweight and obese infertile women who participated in a LIP; clinical useful intervention or patient-related factors associated with dropout could not be identified.

WHAT IS KNOWN ALREADY: Overweight and obese infertile women might improve their chance of conception when they improve their lifestyle and lose weight. Dropout from LIPs reduces the chance of losing considerable weight and is therefore considered to be an important limiting factor of the success of LIPs.

STUDY DESIGN, SIZE, DURATION: This systematic review included 15 studies published between January 1980 and December 2012.

PARTICIPANTS/MATERIALS, SETTING, METHODS: The included studies investigated the effect of LIPs for overweight and obese infertile women with infertility. From these studies, dropout rates and intervention- and patient-related baseline factors associated with dropout, as well as weight loss and pregnancy rates, were recorded.

MAIN RESULTS AND THE ROLE OF CHANCE: There were 15 studies identified, of which 10 reported dropout rates. The median dropout rate was 24% (range: 0–31%). Four studies reported baseline characteristics of women who dropped out, but modifiable predictors of dropout could not be identified. Weight loss and pregnancy rates were lower in women who dropped out than in women who completed the LIPs.

LIMITATIONS, REASONS FOR CAUTION: There were limited numbers of studies investigating patient-related factors associated with dropout. The heterogeneity in the studies precluded us from drawing firm conclusions on the relation between the type of intervention and dropout.

WIDER IMPLICATIONS OF THE FINDINGS: Dropout from LIPs is a major drawback because it predisposes to less weight loss and lower pregnancy rates. Identification of predictors of dropout is needed to identify overweight and obese infertile women who are prone for dropout. These women might benefit from extra support and monitoring, to potentially increasing adherence rates, weight loss and pregnancy chances.

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Key words: dropout / overweight / infertility / lifestyle program

Introduction

Overweight [body mass index (BMI) 25–29.9 kg/m²] and obese (BMI ≥ 30 kg/m²) women have reduced chances of spontaneous conception and lower success rates with fertility treatment (Gesink Law et al., 2007; Maheshwari et al., 2007; Ramlau-Hansen et al., 2007; van der Steeg et al., 2008; Bellver et al., 2010). It has been shown that losing weight can improve the chance of conception in this specific patient category (Clark et al., 1998; Huber Buchholz et al., 1999; Miller et al., 2008). Overweight and obese infertile women are therefore advised to participate in lifestyle intervention programs (LIPs) to lose weight before entering fertility programs (National Institute for Clinical Excellence, 2004).

In LIPs designed for overweight and obese men and women to diminish long-term health risks, dropout rates have been reported to be up to 77% (Davis and Addis, 1999; Honas et al., 2003; Inelmen et al., 2005; Finley et al., 2007). This is considered as an important limiting factor in the success of LIPs because dropout is related to little weight change (Finley et al., 2007). Hence, identifying patients at risk of dropping out might contribute to the development of strategies to increase adherence rates. In LIPs addressing metabolic health risks of obesity in men and women, research has focused on patient-related factors associated with increased dropout risk. Socio-demographic factors including full-time employment, psychological factors such as depression and lower quality of life and behavioral factors like smoking have all been shown to be associated with increased dropout rates and might therefore be considered as predictors for dropout (Clark et al., 1996; Teixeira et al., 2004; Inelmen et al., 2005).

Not only patient-related factors, but also the type of intervention may influence the dropout risk. In a meta-analysis on the long-term effect of structured weight-loss programs, it was demonstrated that very low calorie diets, in which an intake of less than 800 kcal per day was advised, led to higher dropout rates than diets in which subjects were advised to lower their calorie intake by 600 kcal per day (Anderson et al., 2001).

Due to the emotional and social burden of infertility (Greil, 1997), combined with the short-term goal of conception, it is conceivable that overweight and obese infertile women are more motivated to achieve weight loss than women and men who have to lose weight for long-term health improvement. However, dropout rates in LIPs for overweight and obese infertile women have not been systematically reported and little is known about intervention- and patient-related baseline factors associated with dropout in this specific patient population.

We therefore systematically reviewed the literature on LIPs in overweight and obese infertile women to investigate dropout rates and to identify possible intervention- and patient-related factors associated with dropout. In addition, we aimed to compare weight loss and pregnancy rates between overweight and obese infertile women who dropped out of the LIPs and women who completed these programs, to estimate the effect of dropout on these important clinical outcome measures.

Materials and Methods

We searched PubMed, Embase and the Cochrane Library for studies, published in the English literature between January 1980 and December 2012, investigating the effect of LIPs in overweight and obese infertile women.

Women with chronic anovulation or ovulatory women who had tried to conceive for at least 1 year were defined as infertile. Search terms used included BMI, overweight, obesity, infertility, polycystic ovary syndrome (PCOS), lifestyle, intervention program, diet, exercise and weight loss (see Supplementary data, Appendix SI for the full list of key words).

Two reviewers independently screened titles and abstracts of all retrieved studies (M.A.Q.M. and W.K.H.K.). Full text reports of all studies that were likely to investigate the effect of LIPs in overweight and obese infertile women were obtained. Reviews were excluded. The references of the selected articles were checked for relevant and related publications. We attempted to contact the authors for additional information, if deemed necessary. Studies in which it was unclear whether the patient population tried to conceive and studies in which birth control was advised during the intervention program were excluded.

We extracted information on study design, number of participants, baseline BMI, design of the LIP, mean weight loss in completers and dropouts, spontaneous pregnancy rates during the LIP and during follow-up of the LIP, dropout rates and reasons for dropout. Dropout was defined as withdrawal from the program before completing the LIP. Women who discontinued the LIP because of pregnancy were not considered as women who dropped out.

To evaluate a possible association between the type of intervention and dropout and pregnancy rates, we extensively mapped the LIP designs of the included studies. Different study arms were compared to detect possible associations between a specific type of intervention and dropout and pregnancy rates. In addition, possible associations between baseline patient characteristics and dropout reported in all included studies were investigated.

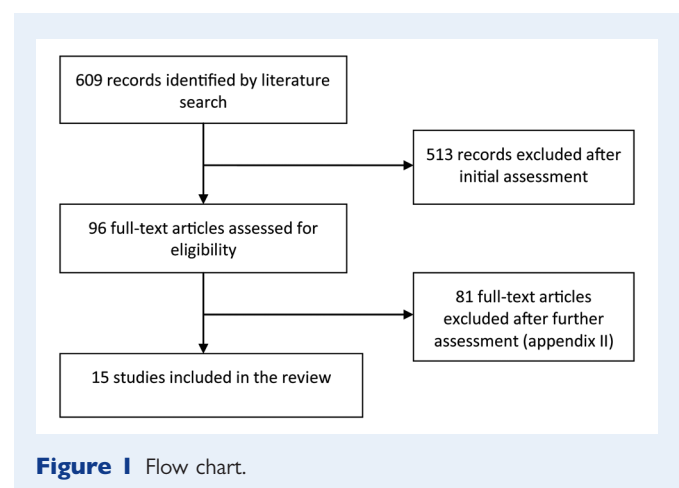
Disagreement was resolved by discussion and consensus. If consensus could not be reached, a third reviewer (A.H.) was consulted.

Statistics

The weighted average, which corrects for sample size, was used to compare pregnancy and dropout rates between the different types of intervention of the included studies.

Results

Our initial literature search generated 609 studies (Fig. 1). After screening the titles and abstracts, 96 articles were identified as potentially eligible. After reading these full-text publications, 81 articles were



excluded (see separate reference list in Supplementary data, Appendix S2), whereas data of the remaining 15 studies were included and subsequently analyzed. Table 1 summarizes the detailed content of the included studies. Data reported in Table 1 were extracted from the original articles. Of the 15 included studies, 13 were prospective cohort studies and two were RCTs. The participants were overweight and obese infertile women with a BMI ranging from 27 up to 43 kg/m². The median duration of the programs was 24 weeks (range 6–32 weeks). Of the 15 included studies, 14 reported pregnancy rates: the median pregnancy rate was 23% (range 1–56%). The amount of weight loss in the included studies could not be summarized, as this was not reported in a consistent way. Ten studies reported dropout rates: the median dropout rate was 24% (range 0–31%). Three studies provided reasons for dropout.

Type of intervention and dropout

We extensively mapped the LIP designs of the included studies; different study arms within the studies were thereby allocated to the different intervention strategies.

- (i) Dietary regimen alone ($n = 6$): In total, 118 women participated, of whom 32 women conceived (weighted average 6%, 1 program did not report pregnancy rates), whereas 20 dropped out (weighted average 4%, 3 programs did not report dropout rates). The median duration of these programs was 24 weeks (range 6–24 weeks) (Bates and Whitworth, 1982; Harlass et al., 1984; Bützow et al., 2000; Crosignani et al., 2003; Qublan et al., 2007; Palomba et al., 2008).
- (ii) Dietary regimen combined with exercise program ($n = 8$): In total, 310 women participated, of whom 56 women conceived (weighted average 11%), whereas 96 women dropped out (weighted average 7%; 2 programs did not report dropout rates). The median duration of the programs was 24 weeks (range 6–32 weeks) (Andersen et al., 1995; Hollmann et al., 1996; Clark et al., 1998; Huber Buchholz et al., 1999; Miller et al., 2008; Karimzadeh and Javedani, 2010; Palomba et al., 2010; Kuchenbecker et al., 2011).
- (iii) Structured exercise program ($n = 1$): In total, 20 women participated in this program and 7 conceived (35%), whereas 3 women dropped out (15%). The duration of the program was 24 weeks (Palomba et al., 2008).
- (iv) Dietary regimen, exercise program and medication or a placebo ($n = 3$): In total, 175 women participated, of whom 9 conceived (weighted average 3%), whereas 17 women dropped out (weighted average 7%). The median duration was 24 weeks (range 6–24 weeks) (Tang et al., 2006; Palomba et al., 2010).
- (v) Medication only ($n = 5$): In total, 322 women participated of whom 43 women conceived (weighted average 11%). Only one study reported dropout rates (no dropout). The median duration was 18 weeks (range 3–24 weeks) (Qublan et al., 2007; Karimzadeh and Javedani, 2010; Palomba et al., 2010).

Baseline characteristics of participants associated with dropout

In four studies, baseline characteristics of dropouts were described. Kuchenbecker et al. (2011) found higher free testosterone and total testosterone levels in women who dropped out (Kuchenbecker

et al., 2011). Clark et al. (1998) did not observe different baseline characteristics in dropouts and completers, but showed that dropouts underwent significantly less cycles of fertility treatment prior to the LIP, when compared with women who completed the LIP (Clark et al., 1998). Tang et al. (2006) could not demonstrate any differences in baseline characteristics between completers and dropouts (Tang et al., 2006). Crosignani et al. (2003) defined dropout as not losing weight within 6 months. They investigated baseline patient characteristics that might predict weight loss and found that the fat mass ratio was the only anthropometric variable that was significantly associated with the probability of losing weight: the lower the basal ratio, the higher the probability of losing weight (Crosignani et al., 2003).

Weight loss and pregnancy rates in dropouts

Three studies reported the amount of weight loss and/or pregnancy rates in women who dropped out (Clark et al., 1998; Crosignani et al., 2003; Kuchenbecker et al., 2011). These studies showed that completers lost more weight than dropouts. In addition, none of the dropouts conceived spontaneously during or within the month after dropout (Table 1).

Discussion

We performed a systematic review on dropout rates and intervention and patient-related baseline factors associated with dropout in LIPs for overweight and obese infertile women. We identified 15 studies, of which 10 studies provided data on dropout. In these studies, a median dropout rate of 24% was observed. Lower dropout rates have been reported in studies with a relatively short-time frame (6 weeks) and substantial higher dropout rates are reported in studies with longer lasting LIPs (see Table 1). As adherence to a LIP is associated with increased weight loss and it is essential for a LIP to be successful (Dansinger et al., 2005), dropout rates up to 24% should be considered representative. Four studies reported baseline characteristics of women who dropped out. Although no clinically useful and modifiable predictors for dropout could be identified in these studies, it was shown that dropouts lost less weight than completers and that they did not conceive spontaneously during or within 1 month after dropout.

From these data, it can be concluded that dropout in LIPs for overweight and obese infertile women is a clinically important problem. Therefore, it is important to identify modifiable predictors for dropout, as this might contribute to the development of tailored strategies, thereby improving adherence of participants to LIPs (Fabricatore et al., 2009).

To the best of our knowledge, this systematic review is the first review in which dropout rates and factors leading to dropout from LIPs are investigated in overweight and obese infertile woman. A drawback of the current review is the difficulty of comparing the LIPs due to the heterogeneity of the available studies. Another drawback is the limited numbers of studies that investigated the association between patient-related baseline factors and dropout, whereas none of the included studies investigated the association between intervention-related factors and dropout.

To overcome these drawbacks, we aimed to detect associations between intervention-related factors and dropout by comparing the

Table 1 Characteristics of the included studies.

Study	Study design	Participants	Baseline BMI of all participants (kg/m ²)	Intervention	Weight loss and spontaneous pregnancy rates in completers	Dropout rates, weight loss and pregnancy rates in dropouts
(Bates and Whitworth, 1982)	Prospective cohort study	18 infertile women with PCOS	28.8 (mean)	Dietary regimen designed to decrease body weight at the rate of 500 g per week Guidance of a therapeutic dietician	Weight loss: 9.6 kg Pregnancy rates: 56% (<i>n</i> = 10)	28% (<i>n</i> = 5) Reasons: not reported Weight loss: not reported Pregnancy rates: not reported
(Bützow et al., 2000)	Prospective cohort study	10 infertile women	37.1 ± 3.3 (mean, SEM)	6-weeks very low calorie diet consisting of 650 kcal/day followed by a 4-week recovery period (normocaloric diet)	Weight loss: 11% weight reduction (mean BMI -4.1 kg/m ²) Pregnancy rates: not reported	No information on dropout was reported
(Crosignani et al., 2003)	Prospective cohort study	33 infertile women with PCOS	32.1 ± 4.2 (mean, SD)	24-weeks dietary regimen consisting of a diet containing 1200 kcal per day Aerobic exercise was recommended Regular controls and weight assessment were carried out every 6–8 weeks	Weight loss: 25 women lost 5% of initial weight Pregnancy rates: 30% (<i>n</i> = 10) within 12 months	24% (<i>n</i> = 8) Reasons: did not reach 5% weight loss within 6 months Weight loss: not reported Pregnancy rates: 0%
(Harlass et al., 1984)	Prospective cohort study	6 infertile women with irregular or absent menses	43 (mean)	16–24 weeks dietary regimen consisting of a calorie-restricted diet of 500 kcal/day. All patients were followed weekly by the authors	Weight loss: 7–12% weight loss (range) Pregnancy rates: 33% (<i>n</i> = 2) within 6 months after study termination	No information on dropout was reported
(Palomba et al., 2008)	Prospective cohort study 2 study arms	40 infertile women with PCOS: 1. 20 2. 20	1. 33.1 ± 1.3 2. 33.2 ± 1.4 (mean, SD)	1. 24-week structured exercise program (SET): 3 training sessions per week consisting of 30 min exercising on a bicycle ergometer 2. 24-week hypocaloric hyperproteic diet aimed at 800 kcal deficit per day in combination with weekly interactive group education meetings	Weight loss (including dropouts) 1. Ovulatory patients (<i>n</i> = 13): 5.6 ± 1.6 kg, anovulatory patients (<i>n</i> = 7): 2.0 ± 0.2 kg 2. Ovulatory patients (<i>n</i> = 5): 10.5 ± 4.1 kg, anovulatory patients (<i>n</i> = 15): 2.3 ± 3.1 kg (mean ± SD) Pregnancy rates: 1. 20% (<i>n</i> = 7) 2. 10% (<i>n</i> = 2)	1. 15% (<i>n</i> = 3) 2. 35% (<i>n</i> = 7) Reasons: not reported Weight loss: not reported Pregnancy rates: not reported
(Qublan et al., 2007)	Prospective comparative study 2 study arms	46 infertile women with PCOS: 1. 24 2. 22	1. 32.2 (29–43) 2. 31.9 (29–44) (mean, range)	24 weeks during program consisting of: 1. A diet containing 1200–1400 kcal per day 2. 850 mg metformin twice a day	Weight loss: not reported BMI change: 1. 4.8 kg/m ² 2. 4.1 kg/m ² Pregnancy rates: 1. 33% (<i>n</i> = 8) 2. 27% (<i>n</i> = 6)	No information on dropout was reported

(Andersen <i>et al.</i> , 1995)	Prospective cohort study	9 women with PCOS (7 women were infertile)	34.1 (28.7–40.7) median (range)	24-weeks dietary regimen consisting of 4 weeks 421 kcal/day and 20 weeks 1000–1500 kcal/day Regularly advice to take a daily walk Monthly examining by a dietician	Weight loss: 2.6 kg after 4 weeks ($n = 9$) 4.8 kg after 24 weeks ($n = 6$) (median) Pregnancy rates: 22% ($n = 2$)	11% ($n = 1$) Reasons: not reported Weight loss: not reported Pregnancy rates: not reported
(Clark <i>et al.</i> , 1998)	Prospective cohort study	87 infertile women	Completers: 37.4 ± 6.9 Dropouts: 35.9 ± 4.1 (mean, SD)	24-weeks group treatment program emphasizing dietary changes and regular exercise containing: 1 h/week exercise with fitness instructor 1 h/week group session with psychiatrist, dietician or reproductive medicine specialist	Weight loss: 6.3 ± 4.2 kg Pregnancy rates: 27% ($n = 18$)	23% ($n = 20$) Reasons: work and other commitments Weight loss: 1.4 ± 1.8 kg (mean ± SD) Pregnancy rates: 0%
(Hollmann <i>et al.</i> , 1996)	Prospective cohort study	35 infertile women	Between 30.8 and 37.3	32-week dietary regimen consisting of regularly advice to reduce weekly intake with 5.000–10.000 kcal Patients were encouraged to increase physical activity	Weight loss: 11.6 kg (median) Pregnancy rates: 29% ($n = 10$)	No information on dropout was reported
(Huber Buchholz <i>et al.</i> , 1999)	Prospective cohort study	28 infertile women with PCOS: 1. 18 anovulatory 2. 10 ovulatory	1. 37.8 ± 0.9 2. 34.6 ± 1.8 (mean, SEM)	24-weeks group treatment program emphasizing dietary changes and regular exercise containing: 1 h/week exercise with fitness instructor 1 h/week group session with psychiatrist, dietician or reproductive medicine specialist	Weight loss: 2–5% of starting weight Pregnancy rates: 1. 11% ($n = 3$) 2. 0	1. 17% ($n = 3$) 2. 40% ($n = 4$) Reasons: not reported Weight loss: not reported Pregnancy rates: not reported
(Karimzadeh and Javedani, 2010)	Prospective randomized double-blind study	343 infertile women with PCOS: 1. 90 2. 90 3. 88 4. 75	1. 27.2 ± 2.9 2. 27.2 ± 1.7 3. 28 ± 1.1 4. 28 ± 1.1 (mean, SD)	1. 100 mg CC on days 3–7 for a maximum of 3–6 cycles 2. 500 mg Metformin® in a step-up dose till 1500 mg/day for 12–24 weeks 3. Combination of CC and Metformin® as described above 4. Lifestyle modification: dietary regimen consisting of a deficit of 500 calories per day when compared with daily requirements in combination with 3–5 times per week 20–60 min exercising	Weight loss: not reported Pregnancy rates: 1. 22% ($n = 11$) 2. 14% ($n = 13$) 3. 14% ($n = 13$) 4. 20% ($n = 15$)	No information on dropout was reported
(Kuchenbecker <i>et al.</i> 2011)	Prospective cohort study	32 infertile women with anovulatory cycles	Completers: 37.8 ± 5.2 Dropout: 36.7 ± 4.3 (mean, SD)	24-week lifestyle program consisting of: individualized dietary advice (reduction in calorie intake of ≥ 500 kcal/day) Individualized exercise program Behavior modification Guidance of a nurse practitioner every 2 weeks	Weight loss: Women who resumed ovulation lost 6.3% of body weight Pregnancy rates: 22% ($n = 7$)	31% ($n = 10$) Reasons: not reported Weight loss: women who remained anovulatory (including dropouts) lost 3.0% of body weight Pregnancy rates: 0%
(Miller <i>et al.</i> 2008)	Prospective cohort study	12 infertile women	≥ 30	12-week lifestyle program consisting of a 1200–1500 kcal/day individualized diet and three times per week fitness sessions of 1 h. Encouraged to exercise independently throughout the week Weekly educational sessions on obesity and infertility	Weight loss: not reported BMI change: –2.1 kg/m ² Pregnancy rates: 8% ($n = 1$)	8% ($n = 1$) Reasons: not reported Weight loss: not reported Pregnancy rates: not reported

Continued

Table I Continued

Study	Study design	Participants	Baseline BMI of all participants (kg/m ²)	Intervention	Weight loss and spontaneous pregnancy rates in completers	Dropout rates, weight loss and pregnancy rates in dropouts
(Palomba et al. 2010)	Parallel controlled assessor-blinded RCT 3 study arms	96 CC-resistant infertile women with PCOS: 1. 32 2. 32 3. 32	1. 31.3 ± 2.7 2. 32.3 ± 3.7 3. 31.1 ± 3.0 (mean, SD)	1. 6-weeks during SET: 3 training sessions per week consisting of 30 min cycling and hypocaloric hyperproteic diet aimed at 1000 kcal deficit per day 2. After 2 weeks of observation, 150 mg CC was given daily for 5 days (in absence of ovarian response) 3. 6-week during SET and hypocaloric hyperproteic diet aimed at 1000 kcal deficit per day. After 2 weeks, 150 mg CC was added daily for 5 days (in absence of ovarian response)	Weight loss: not reported BMI change: 1. 2.4 kg/m ² 2. -0.06 kg/m ² 3. 2.64 kg/m ² (mean) Pregnancy rates: 1. 0 2. 0 3. 3% (n = 1)	1. 0 2. 0 3. 0
(Tang et al. 2006)	Placebo-controlled double-blind RCT 2 study arms	143 infertile women with PCOS: 1. 69 women 2. 74 women	1. 37.6 ± 5.0 2. 38.9 ± 9.5 (mean, SD)	24-weeks lifestyle modification program consisting of: Standardized high-carbohydrate low-fat diet aimed at 500 kcal reduction/day Encouraging to increase daily exercise by 15 min Monthly visits with a research dietician In combination with: 1. Metformin® 850 mg twice a day 2. Placebo medication twice a day	Weight loss: 1. 2.8 kg (1.8–3.9) 2. -1.5 kg (-0.3 to 2.6)(mean, 95% CI) Pregnancy rates: 1. 9% (n = 6) 2. 3% (n = 2)	1. 16% (n = 11) 2. 8% (n = 6) Reasons: side effects Weight loss: not reported Pregnancy rates: not reported

BMI, body mass index; PCOS, polycystic ovarian syndrome; SEM, standard error of the mean; SD, standard deviation; RCT, randomized controlled trial; SET, structured exercise program; CC, clomiphene citrate.

different types of intervention of the included studies. Our comparison showed comparable dropout rates in LIPs consisting of a dietary regimen only and in LIPs in which a dietary regimen was combined with an exercise program (weighted average 4 and 7%, respectively). However, the large heterogeneity in study design, duration of the LIPs and heterogeneous description of the results in the studies precluded us from drawing firm conclusions on the association between the type of intervention and risk of dropout.

Modifiable predictors for dropout could not be identified. This is in concordance with the findings in a large cohort of 114 obese women with PCOS in which [Ladson et al. \(2011\)](#) investigated whether the combination of a LIP and Metformin® was better in improving the PCOS phenotype than a LIP in combination with placebo ([Ladson et al., 2011](#)). They could not identify any association between dropout and baseline factors such as BMI, hormone levels, lipid parameters, ultrasound parameters and psychosocial baseline factors.

Identifying patients at risk for dropout does not only rely on patient-related baseline factors. In a 6-month weight loss intervention study in 137 post-menopausal obese women, it was suggested that an unsatisfactory or slow rate of weight loss, especially in the beginning of a weight loss program, is also associated with dropout ([Messier et al., 2010](#)). Participants who are not losing weight might be discouraged and have increased their risk of dropout. Understanding the possible reasons for the slower rate of weight loss may help to improve the support of these subjects, especially during the start of the LIP ([Messier et al., 2010](#)). Furthermore, weight loss expectations have been shown to be independent cognitive predictors of dropout during weight loss programs: higher expectations at baseline lead to higher dropout rates ([Dalle Grave et al., 2005](#)). Self-efficacy, which is faith in oneself, might play a crucial role in this process ([Cochrane, 2008](#)). Patients with high self-efficacy may attach themselves to goals that are not realistically achievable that, in turn, might lead to a 'false hope syndrome': a phenomenon that is characterized by unrealistic expectations of self-change attempts ([Polivy, 2001](#); [Jones et al., 2005](#)). On the other hand, patients with an external locus of control will have low self-efficacy, and it may be hypothesized that these patients are prone for dropout as well ([Cochrane, 2008](#)). Studies assessing self-efficacy of participants could help to identify those subjects who are prone for dropout in LIPs for overweight and obese infertile women. Whether initial inadequate weight loss and unrealistic goal setting at baseline can predict dropout should be investigated in this specific population.

In conclusion, our review shows a median dropout rate of 24% in overweight and obese infertile women participating in LIPs. Our data also indicate that women who dropout lose less weight and have lower spontaneous pregnancy chances than completers. We could not identify intervention- or patient-related factors associated with dropout. Future studies should focus on predictors of dropout in this patient population. This will enable the identification of patients who are prone for dropping out and who might benefit from extra support and monitoring to increase adherence rates, weight loss and pregnancy chances.

Supplementary data

Supplementary data are available at <http://humrep.oxfordjournals.org/>.

Authors' roles

All authors were involved in the conception and design of the study. M.A.Q.M. contributed to the data acquisition and analysis and the writing of the manuscript. W.K.H.K. contributed to the data acquisition and analysis. All authors critically reviewed and approved the final manuscript.

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Conflict of interest

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References

- Andersen P, Seljeflot I, Abdelnoor M, Arnesen H, Dale PO, Lvik A, Birkeland K. Increased insulin sensitivity and fibrinolytic capacity after dietary intervention in obese women with polycystic ovary syndrome. *Metabolism* 1995;**44**:611–616.
- Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies. *Am J Clin Nutr* 2001;**74**:579–584.
- Bates GW, Whitworth NS. Effect of body weight reduction on plasma androgens in obese, infertile women. *Fertil Steril* 1982;**38**:406–409.
- Bellver J, Aylln Y, Ferrando M, Melo M, Goyri E, Pellicer A, Remoh J, Meseguer M. Female obesity impairs in vitro fertilization outcome without affecting embryo quality. *Fertil Steril* 2010;**93**:447–454.
- Bützow TL, Lehtovirta M, Siegborg R, Hovatta O, Koistinen R, Sepplä M, Apter D. The decrease in luteinizing hormone secretion in response to weight reduction is inversely related to the severity of insulin resistance in overweight women. *J Clin Endocrinol Metab* 2000;**85**:3271–3275.
- Clark MM, Niaura R, King TK, Pera V. Depression, smoking, activity level, and health status: pretreatment predictors of attrition in obesity treatment. *Addict Behav* 1996;**21**:509–513.
- Clark AM, Thornley B, Tomlinson L, Galletley C, Norman RJ. Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment. *Hum Reprod* 1998;**13**:1502–1505.
- Cochrane G. Role for a sense of self-worth in weight-loss treatments: helping patients develop self-efficacy. *Can Fam Physician* 2008;**54**:543–547.
- Crosignani P, Colombo M, Vegetti W, Somigliana E, Gessati A, Ragni G. Overweight and obese anovulatory patients with polycystic ovaries: parallel improvements in anthropometric indices, ovarian physiology and fertility rate induced by diet. *Hum Reprod* 2003;**18**:1928–1932.
- Dalle Grave R, Calugi S, Molinari E, Petroni M, Bondi M, Compare A, Marchesini G. Weight loss expectations in obese patients and treatment attrition: an observational multicenter study. *Obes Res* 2005;**13**:1961–1969.

- Dansinger M, Gleason J, Griffith J, Selker H, Schaefer E. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA* 2005;**293**:43–53.
- Davis MJ, Addis ME. Predictors of attrition from behavioral medicine treatments. *Ann Behav Med* 1999;**21**:339–349.
- Fabricatore A, Wadden T, Moore R, Butryn M, Heymsfield S, Nguyen A. Predictors of attrition and weight loss success: Results from a randomized controlled trial. *Behav Res Ther* 2009;**47**:685–691.
- Finley CE, Barlow CE, Greenway FL, Rock CL, Rolls BJ, Blair SN. Retention rates and weight loss in a commercial weight loss program. *Int J Obes* 2007;**31**:292–298.
- Gesink Law DC, Maclehose RF, Longnecker MP. Obesity and time to pregnancy. *Hum Reprod* 2007;**22**:414–420.
- Greil AL. Infertility and psychological distress: a critical review of the literature. *Soc Sci Med* 1997;**45**:1679–1704.
- Harlass FE, Plymate SR, Fariss BL, Belts RP. Weight loss is associated with correction of gonadotropin and sex steroid abnormalities in the obese anovulatory female. *Fertil Steril* 1984;**42**:649–652.
- Hollmann M, Runnebaum B, Gerhard I. Effects of weight loss on the hormonal profile in obese, infertile women. *Hum Reprod* 1996;**11**:1884–1891.
- Honas J, Early J, Frederickson D, O'Brien M. Predictors of attrition in a large clinic-based weight-loss program. *Obes Res* 2003;**11**:888–894.
- Huber Buchholz MM, Carey DG, Norman RJ. Restoration of reproductive potential by lifestyle modification in obese polycystic ovary syndrome: role of insulin sensitivity and luteinizing hormone. *J Clin Endocrinol Metab* 1999;**84**:1470–1474.
- Inelmen EM, Toffanello ED, Enzi G, Gasparini G, Miotto F, Sergi G, Busetto L. Predictors of dropout in overweight and obese outpatients. *Int J Obes* 2005;**29**:122–128.
- Jones F, Harris P, Waller H, Coggins A. Adherence to an exercise prescription scheme: the role of expectations, self-efficacy, stage of change and psychological well-being. *Br J Health Psychol* 2005;**10**:359–378.
- Karimzadeh M, Javedani M. An assessment of lifestyle modification versus medical treatment with clomiphene citrate, metformin, and clomiphene citrate-metformin in patients with polycystic ovary syndrome. *Fertil Steril* 2010;**94**:216–220.
- Kuchenbecker WKH, Groen H, van Asselt S, Bolster JHT, Zwerver J, Slart RHJ, Vd Jagt E, Muller Kobold A, Wolffenbuttel BHR, Land J et al. In women with polycystic ovary syndrome and obesity, loss of intra-abdominal fat is associated with resumption of ovulation. *Hum Reprod* 2011;**26**:2505–2512.
- Ladson G, Dodson W, Sweet S, Archibong A, Kunselman A, Demers L, Williams N, Coney P, Legro R. The effects of metformin with lifestyle therapy in polycystic ovary syndrome: a randomized double-blind study. *Fertil Steril* 2011;**95**:1059–66.e1.
- Maheshwari A, Stofberg L, Bhattacharya S. Effect of overweight and obesity on assisted reproductive technology—a systematic review. *Hum Reprod Update* 2007;**13**:433–444.
- Messier V, Hayek J, Karelis AD, Messier L, Doucet E, Prud'homme D, Rabasa-Lhoret R, Strychar I. Anthropometric, metabolic, psychosocial and dietary factors associated with dropout in overweight and obese postmenopausal women engaged in a 6-month weight loss programme: a MONET study. *Br J Nutr* 2010;**103**:1230–1235.
- Miller P, Forstein D, Styles S. Effect of short-term diet and exercise on hormone levels and menses in obese, infertile women. *J Reprod Med* 2008;**53**:315–319.
- National Institute for Clinical Excellence. *Fertility: Assessment and Treatment for People with Fertility Problems*. London: National Institute for Clinical Excellence (NICE), 2004.
- Palomba S, Giallauria F, Falbo A, Russo T, Oppedisano R, Tolino A, Colao A, Vigorito C, Zullo F, Orio F. Structured exercise training programme versus hypocaloric hyperproteic diet in obese polycystic ovary syndrome patients with anovulatory infertility: a 24-week pilot study. *Hum Reprod* 2008;**23**:642–650.
- Palomba S, Falbo A, Giallauria F, Russo T, Rocca M, Tolino A, Zullo F, Orio F. Six weeks of structured exercise training and hypocaloric diet increases the probability of ovulation after clomiphene citrate in overweight and obese patients with polycystic ovary syndrome: a randomized controlled trial. *Hum Reprod* 2010;**25**:2783–2791.
- Polivy J. The false hope syndrome: unrealistic expectations of self-change. *Int J Obes* 2001;**25**(Suppl 1):S80–S84.
- Qublan H, Yannakoula E, Al Qudah M, El Uri F. Dietary intervention versus metformin to improve the reproductive outcome in women with polycystic ovary syndrome. A prospective comparative study. *Saudi Med J* 2007;**28**:1694–1699.
- Ramlau-Hansen CH, Thulstrup AM, Nohr EA, Bonde JP, Sorensen TI, Olsen J. Subfecundity in overweight and obese couples. *Hum Reprod* 2007;**22**:1634–1637.
- Tang T, Glanville J, Hayden C, White D, Barth J, Balen A. Combined lifestyle modification and metformin in obese patients with polycystic ovary syndrome. A randomized, placebo-controlled, double-blind multicentre study. *Hum Reprod* 2006;**21**:80–89.
- Teixeira PJ, Going SB, Houtkooper LB, Cussler EC, Metcalfe LL, Blew RM, Sardinha LB, Lohman TG. Pretreatment predictors of attrition and successful weight management in women. *Int J Obes* 2004;**28**:1124–1133.
- van der Steeg JW, Steures P, Eijkemans MJ, Habbema JD, Hompes PG, Burggraaff JM, Oosterhuis GJ, Bossuyt PM, van der Veen F, Mol BW. Obesity affects spontaneous pregnancy chances in subfertile, ovulatory women. *Hum Reprod* 2008;**23**:324–328.